REMARKS

The above-noted amendments to the claims are respectfully submitted in connection with applicants' filing of a Continued Prosecution Application. The amendments are also further to the advisory action dated February 27, 2002, in applicants' parent application, and a subsequent telephone interview between applicants' counsel and Examiner Webman respecting same. During that discussion, applicants once again emphasized the nature and substance of the present invention, and the various preferred embodiments thereof which are exemplified in the amended claims now set forth herein. In view of the status of the prosecution of the parent application, however, it was necessary to file a Continued Prosecution Application, although the Examiner agreed to consider any amendment filed by applicants. Applicants therefore express their appreciation for the Examiner's position in this regard.

The sole barrier to allowance of applicants' prior claims has been the citation of Miranda *et al.* under the provisions of 35 U.S.C. § 102(b). The Examiner takes the position that Miranda *et al.* teaches a transdermal comprising an active and a mixture of polymers; namely, an acrylate polymer and a polysiloxane, and that tetracaine and chlorpheniramine are specified, citing column 11, lines 5 and 25 thereof. This rejection is respectfully traversed in view of the above amendments and arguments and for the reasons set forth hereinafter.

Applicants continue to emphasize the fact that both the overall nature and the specific claimed aspects of the present invention are readily distinguishable from anything in Miranda *et al.*, and that these claims clearly define patentable subject matter thereover.

The specific aspect of the invention disclosed in this application which is the subject of the pending claims herein

relates to a device which overcomes a number of problems surrounding the production of transdermal patches, and in particular those which utilize certain highly plasticizing drugs. Thus, when these types of drugs are loaded into an adhesive system, they are known to have a definite adverse impact on the adhesive properties thereof. The plasticizing effect of these drugs can thus have significant deleterious effects on the physical properties of these adhesive matrices. As is spelled out in the present specification, while there are a large number of such adhesive systems which are well known in this art, including highly cross-linked systems, actual observation has unexpectedly revealed highly inconsistent results with their ability to provide adhesive matrix systems which can accommodate these highly plasticizing drugs to any truly useful extent. As is thus shown on page 5 of the specification, upon preparing mixtures of one of these highly plasticizing drugs (namely, selegeline) at a level of 15 wt.%, with various commercially known acrylic adhesive systems, the polken tack results obtained initially appeared to be acceptable for all of these drugs as follows:

TABLE 1

POLKEN TACK OF VARIOUS

TRANSDERMAL ADHESIVES WITH 15% SELEGILINE

ADHESIVE	POLKEN TACK
GELVA 1753	346
DUROTAK 87-2194	453
GELVA 737	333
DUROTAK 87-2516	286

However, when these formulations were actually tried on the skin, the results were far less definitive. Indeed, some of these formulations did not work, and unexpectedly exhibited significant cohesive failure in which adhesive remained on the

skin after the patch had been peeled off. For example, such patches made with both DUROTAK 87-2194 and GELVA 2655 exhibited adhesive failure. When shear strength was then measured, the results were further inconsistent. (*See* page 6 of the specification.) For example, DUROTAK 87-2516 exhibited acceptable shear, while the formulation thereof was totally unacceptable.

In accordance with the present invention, the inventors have quite unexpectedly discovered that highly plasticizing drugs can be used, at significant levels, with a particular class of acrylic polymeric adhesives. These adhesives are the subject of the present claims, which also specifically require that they be used in a system which is substantially free of water and liquids having a normal boiling point which is both below the processing temperatures used for these transdermal delivery systems and equal to or greater than the normal boiling points of the low molecular weight drugs themselves. It is only in these systems, as defined by the present claims, that one is now able to provide transdermal delivery systems which incorporate these highly plasticizing drugs and at the same time maintain acceptable adhesive properties. Nothing in the prior art suggests this invention.

Turning to Miranda *et al.*, the invention set forth in this reference relates to the use of two or more polymers in a blend in which the polymers have different solubility parameters and are preferably immiscible, for the purpose of adjusting the solubility of a drug in the adhesive system formed thereby. Thus, in a preferred embodiment of Miranda *et al.*, a polyacrylate and polysiloxane system is employed to control the overall solubility parameter thereof. This is the crux of the Miranda *et al.* patent, while the patentees go on to then describe the incorporation of known accelerants, skin penetration enhancers, and other co-solvents in the multiple

polymer systems thereof. Applicants respectfully submit that there is no recognition whatsoever of the nature and substance of the present invention in Miranda *et al.*, and that at best the Examiner is reconstructing the claimed invention hereof by selecting various elements of the Miranda *et al.* patent without guidance; indeed, in a manner which is actually contrary to the requirements of that patent.

In the first instance, the present claims are limited to transdermal delivery systems consisting essentially of the blends set forth in claims 84, 92, and the dependent claims thereon. These blends consist essentially of an acrylic-based polymer, while it is clear that an essential requirement of Miranda *et al.* is at least two polymers therein, so that even in those cases where one of Miranda *et al.*'s polymers is a polyacrylate, the blend still requires, as an essential component thereof, a second polymer, which is not within the purview of the present claims. Secondly, there is no teaching in Miranda *et al.* that the present results can be achieved by requiring that the transdermal delivery system be substantially free of the solvents set forth in claims 84 and 92 hereof. To the contrary, the teachings of Miranda *et al.* clearly prefer the use of solvents excluded from the present claims, such as propylene glycol and the like, which are exemplified throughout the Miranda *et al.* specification. Applicants once again submit that, as is clearly demonstrated by the specific data set forth in this application, it is only by limiting these transdermal delivery systems to the specific acrylic polymers which are the subject of these claims, and by specifically excluding the solvents which are excluded by these claims, that one is able to obtain transdermal delivery systems which include these highly plasticizing drugs in significant commercial amounts while maintaining the properties of these adhesive systems. Nothing of this kind is suggested by Miranda *et al.*

In addition to all of the above, reference can also be made to the additional dependent claims which are now included in this application. As is highlighted throughout the present specification, the preferred embodiments hereof in which the acrylic-based polymers include a C_4-C_{12} alkyl acrylate are not recognized by Miranda *et al.* Indeed, there is no teaching to this effect. This is not surprising, however, since Miranda *et al.* did not appreciate the nature and substance of the present invention. Even more particularly, when these systems are combined with a C_1-C_4 alkyl acrylate hardening monomer (claim 87), an even more preferred embodiment is obtained. Furthermore, when a functionalizing monomer is included (claim 88), and a cross-linking agent is added thereto (claim 89), an even more preferred embodiment of the present invention is exemplified herein. None of this is, of course, suggested by Miranda *et al.*

It is finally noted that in an advisory action dated February 27, 2002, in applicants' parent application, the Examiner had argued that applicants have not claimed highly plasticizing drugs at high concentrations and adhesive formulations. Applicants respectfully submit that this is clearly not the case, at least in view of the above amendments. All of the claims in this application now specifically require certain drugs which have a low molecular weight and which are liquid at or about room temperature, to wit the highly plasticizing drugs hereof. It is further noted that newly added claim 90 specifies the low molecular weight to the degree set forth in the specification at page 13, line 25 hereof. Furthermore, it is applicants' position that the specification demonstrates that these drugs can be used at high concentrations because of the claimed system hereof. However, it is noted that claim 91 has been added to specify the amount of these drugs. Finally, the adhesive formulations hereof are the real substance

of this invention, and are clearly also set forth in these claims.

It is therefore respectfully submitted that the claims presently set forth in this application clearly possess the requisite novelty, utility and unobviousness to warrant their immediate allowance, and such action is therefore respectfully solicited. If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he telephone applicant's attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: April 18, 2002

Respectfully submitted,

By_____

Arnold H. Krumholz
Registration No.: 25,428
LERNER, DAVID, LITTENBERG,
KRUMHOLZ & MENTLIK, LLP
600 South Avenue West
Westfield, New Jersey 07090
(908) 654-5000
Attorneys for Applicant

MARKED-UP COPY OF AMENDED CLAIMS:

84. (THREE TIMES AMENDED) A transdermal delivery system consisting essentially of a blend of:

(a) one or more hydrophobic polymers acrylic-based polymers; and

(b) a therapeutically effective amount of one or more drugs, at least one of which is of low molecular weight and liquid at or about room temperatures,

wherein said system is substantially free of water and liquids having a normal boiling point (i) below processing temperatures and (ii) equal to or greater than the normal boiling points of the low molecular weight drugs.